Feature

Key reflections

The 50th anniversary of the publication of Watson and Crick's structure for DNA last year spawned many events and a new book of essays adds to the material future historians will pore over in evaluating the significance of this achievement. **Nigel Williams** reports.

DNA

Edited by Torsten Krude
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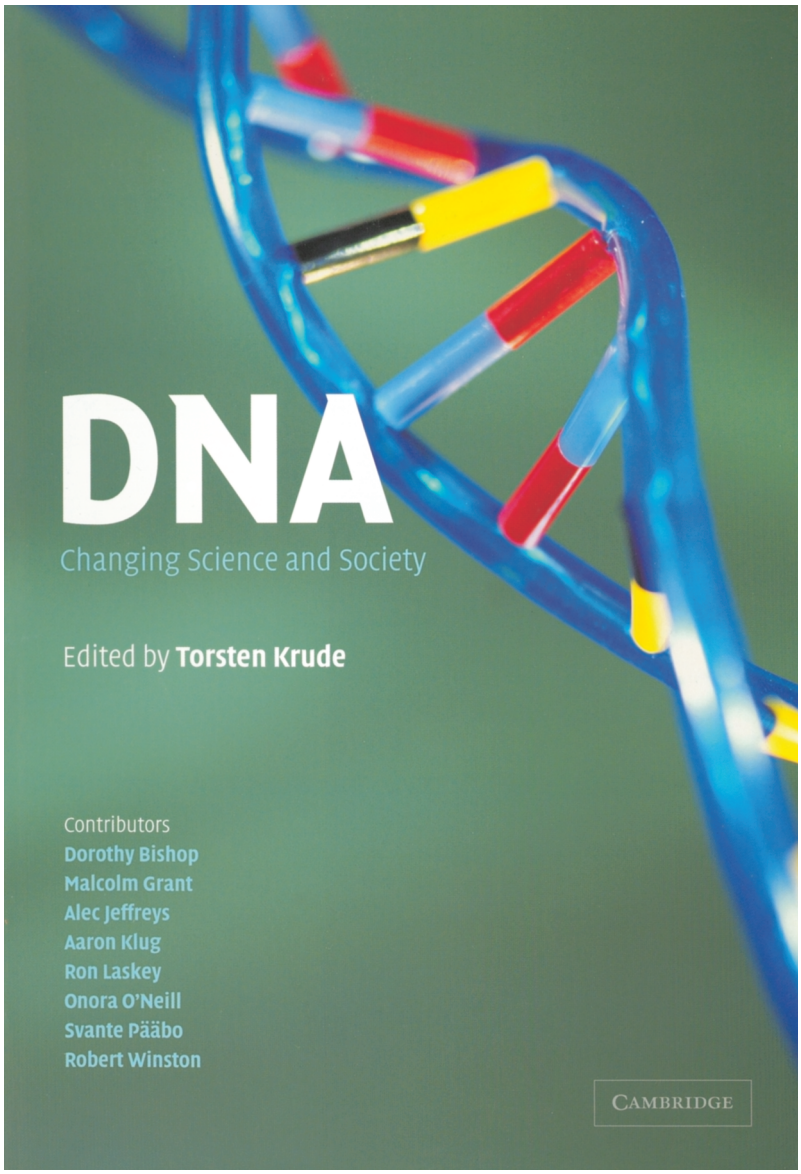
The 50th anniversary of the publication of the proposed double-helix structure for DNA by James Watson and Francis Crick last year was widely celebrated. But historically, we are still perhaps too close to the event to realise its ultimate significance. Therefore, the more people who were involved or who subsequently worked with the molecule write and tell of their experiences, the richer history will eventually be. A new book, based on a series of lectures given last year at Darwin College, Cambridge, edited by Torsten Krude, provides much valuable information.

Darwin published his theory to account for the extraordinary variety of species found on this planet almost exactly 100 years before Crick and Watson announced the structure of chromosomal DNA. The theory of natural selection provoked immediate and passionate debate and caused outrage in some sections of society. By contrast, knowledge of the structure of DNA has already led to many developments in research, agriculture and medicine, and has widespread practical uses, whereas it is only now that the social effects are becoming important.

In view of the wide range of techniques now available for the detection and manipulation of DNA and the number of uses to which they are put, it is clear that eight essays can provide only a glimpse into their chosen subjects. Inevitably there are aspects that are not discussed. In this context, it is surprising that there is no essay on methods of sequencing or on the value of the genomic sequences. Current projects to describe the entire genome of different species depend on being able to determine the sequence of nucleotides in a fragment of DNA. Fred Sanger, working in Cambridge, devised the method that is still in use today and for which he was awarded his second Nobel prize in 1980. Within a mere 15 years, an international collaboration obtained the first



Molecular matters: Reflections on the discovery of the structure of DNA, presented in a series of lectures at Darwin College, Cambridge, last year, form the content of this new book.

complete sequence of the nucleotides in a human genome.

The content of the essays varies considerably. Aaron Klug describes the events that led to the discovery of the structure of DNA. He worked with Rosalind Franklin and had access to her laboratory notebooks and from his contribution it is hard to disagree that Crick and Watson should have acknowledged their use of the data they obtained from Franklin's work more clearly than they did in the 1953 paper.

One of the most interesting contributions is that of Alec Jeffreys, because, as the discoverer of genetic fingerprinting, he has insight into one of the techniques using DNA that has had the greatest social impacts so far. He describes the steps in the development of different methods for DNA fingerprinting at Leicester University and also the first use of the techniques in court. It is well known that these methods are now used for the identification of criminals, but it is interesting to learn that they were first used in 1985 to confirm the genetic relationship between would-be immigrants to Britain. Previously, the official decision had depended on a subjective judgement by an immigration officer based on documents and appearance.

"This technology has directly impacted on the lives of countless thousands of people involved in criminal investigations, paternity disputes, immigration challenges and the like," Jeffreys says.

"The key experiment in September 1984 was a small test of a range of samples that included, for no particular good reason, DNA from a human father/mother/child trio as well as DNA from a baboon, a seal, a cow, a mouse and a tobacco plant. While the results were hideously murky, it was clear that we were detecting lots of what appeared to be highly variable DNA fragments. Mum and dad were obviously different, and the child seemed to be a union of the parents' DNA patterns. Equally exciting, it looked as if the system worked on other species too."

Jeffreys says, "It was clear that we had accidentally stumbled on a DNA method not only for individualisation but also for establishing family relationships. Thus was DNA fingerprinting born. The one sensible decision we did take was to use the term `DNA fingerprint' rather than the more accurate, if rather incomprehensible, term 'idiosyncratic Southern-blot minisatellite hybridisation profile.' The decision helped bring our work to public attention through the press."

As a result of the press coverage, Jeffreys got a letter from a solicitor in London asking for help in resolving a two-year immigration case involving a Ghanian boy who had been stopped from entering the country on a forged passport. "I said, yes, though I didn't hold out much hope," he later reported. "For one thing, there were still question marks over the statistical independence of the process and, for another, the case was enormously complicated," he said. But identification turned out to be straightforward, and Jeffreys was able to prove that the boy was the woman's daughter and that he and the other children shared the same father. "It was a legally defining moment for genetic fingerprinting," he said.

DNA has also proved to be remarkably stabe in certain environments. Svante Pääbo describes how genetic techniques have provided insights into the evolution of animal species, including humanoids, and into the first breeding of agricultural crop plants. Neanderthals appeared 100,000 years ago and persisted for 70,000 years, during which period our own species emerged. The extent of the interaction between the species is unclear. Studies of variation in mitochondrial DNA suggest that Neanderthal and our own species did not interbreed. Comparable analyses of chromosomal DNA of maize and its ancestors in Mexico suggest that some critical traits were fixed by selection several thousand years ago, early in the process of domestication.

The startling improvements in yield achieved by more recent plant breeding relied on a variety of techniques to cause genetic change and to cross species that would not normally reproduce.

Malcolm Grant of University College London is an advocate of the potential benefits of modern techniques and genetic modification in plant breeding. He describes the various organisations that have been involved in the regulation of genetic modification in agriculture and demonstrates the importance of there being an effective public debate rather than the present polarised situation in many countries including the UK.

Other essays deal with the use of modern molecular biology in aspects of medicine ranging from techniques of assisted reproduction (Robert Winston) to causes of cancer (Ron Laskey). Cancers arise as a result of damage to DNA, but paradoxically, many of our present therapies rely on causing more damage to DNA to induce destruction of the cells. Less familiar is a discussion by Dorothy Bishop of Oxford University of the genes associated with the acquisition of language. Her recent research has begun to identify regions of chromosomes that are associated with the variation in the ability of children to learn new sounds. Difficulty in learning new sounds was associated with an impaired ability to acquire language.

Molecular genetics will contribute so many benefits to society that it is impossible to list them all. But they will certainly include new understanding and, in some cases, treatments for unpleasant diseases. However, these developments bring with them significant risks to individuals and society. Each country will have to determine the appropriate use of new techniques. In the final essay, Onora O'Neill provides a clear analysis of the ethical issues for many of the uses of molecular genetics. She highlights the great need for wider understanding of both the biology and ethical issues.